



SEQUENCE LISTING

<110> Hammock, Bruce D.
Kim, In-Hae
Morisseau, Christophe
Watanabe, Takaho
Newman, John W.
The Regents of the University of California

<120> Improved Inhibitors for the Soluble Epoxide Hydrolase

<130> 02307W-131010US

<140> US 10/817,334
<141> 2004-04-02

<150> US 60/460,559
<151> 2003-04-03

<160> 4

<170> PatentIn Ver. 2.1

<210> 1
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<212> PRT
<213> Homo sapiens

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<223> human soluble epoxide hydrolase (sEH)

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Pro Leu Met Glu Glu Asn Cys Arg Lys Cys Ser Glu Thr Ala Lys Val
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Cys Leu Pro Lys Asn Phe Ser Ile Lys Glu Ile Phe Asp Lys Ala Ile
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Ser Ala Arg Lys Ile Asn Arg Pro Met Leu Gln Ala Ala Leu Met Leu
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Arg Lys Lys Gly Phe Thr Thr Ala Ile Leu Thr Asn Thr Trp Leu Asp
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 <212> PRT
 <213> Rattus norvegicus

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 Pro Asn Glu Val Val Phe Leu Asp Asp Phe Gly Ser Asn Leu Lys Pro
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Tyr	Ile	Gln	Gln	Phe	Lys	Lys	Ser	Gly	Phe	Arg	Gly	Pro	Leu	Asn	Trp	450	455	460
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<212> PRT

<213> Mus musculus

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<223> mouse liver soluble epoxide hydrolase (sEH)

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Pro Leu Met Asp Glu Ser Tyr Arg Lys Ser Ser Lys Ala Cys Gly Ala
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Lys Lys Lys Gly Phe Thr Thr Cys Ile Val Thr Asn Asn Trp Leu Asp
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<212> PRT

<213> Mus musculus

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<223> mouse ovary soluble epoxide hydrolase (sEH)

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Arg Ser Ile Asn Arg Pro Met Leu Gln Ala Ala Ile Ala Leu Lys Lys
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Pro Val Pro Cys Asn Pro Asn Asp Val Ser His Gly Tyr Val Thr Val
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Lys Pro Gly Ile Arg Leu His Phe Val Glu Met Gly Ser Gly Pro Ala
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Ile	Leu	Val	Pro	Ala	Leu	Met	Val	Thr	Ala	Glu	Lys	Asp	Ile	Val	Leu	
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Arg	Pro	Glu	Met	Ser	Lys	Asn	Met	Glu	Lys	Trp	Ile	Pro	Phe	Leu	Lys	
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Asn	Pro	Ser	Val	Thr	Ser	Lys	Ile									
	530					535										



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Feat

☐ 1: AAA37555. epoxide hydrolase...[gi:441071]

BLink, Domains, Links

LOCUS AAA37555 554 aa linear ROD 14-JAN-1994

DEFINITION epoxide hydrolase.

ACCESSION AAA37555

VERSION AAA37555.1 GI:441071

DBSOURCE locus MUSEPOHYDR accession L05781.1

KEYWORDS

SOURCE Mus musculus (house mouse)

ORGANISM Mus musculus

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.

REFERENCE 1 (residues 1 to 554)

AUTHORS Grant,D.F., Storms,D.H. and Hammock,B.D.

TITLE Molecular cloning and expression of murine liver soluble epoxide
hydrolase

JOURNAL J. Biol. Chem. 268 (23), 17628-17633 (1993)

MEDLINE 93352558

PUBMED 8349642

COMMENT Method: conceptual translation.

FEATURES

source

Location/Qualifiers

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/dev_stage="adult"

/germline

Protein

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CDS

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/coded_by="L05781.1:1..1665"

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241 tvkpgirlhf vemgsgpalc lchgfpeswf swryqipala qagfrvlaid mkggydsssp
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//

Aug 4 2004 12:36:34



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Feat

☐ 1: P80299. Soluble epoxide h...[gi:462371]

BLink, Domains, Links

LOCUS P80299 554 aa linear ROD 15-JUN-2004

DEFINITION Soluble epoxide hydrolase (SEH) (Epoxide hydratase) (Cytosolic epoxide hydrolase) (CEH).

ACCESSION P80299

VERSION P80299 GI:462371

DBSOURCE swissprot: locus HYES_RAT, accession P80299;

class: standard.

created: Feb 1, 1994.

sequence updated: Feb 1, 1994.

annotation updated: Jun 15, 2004.

xrefs: gi: 402631, gi: 402632, gi: 55929, gi: 55930, gi: 477003

xrefs (non-sequence databases): HSSPP34914, MEROPSS33.973,

InterProIPR000073, InterProIPR003089, InterProIPR000639,

InterProIPR006402, InterProIPR005833, InterProIPR005834,

InterProIPR000379, PfamPF00561, PfamPF00702, PRINTSPR00111,

PRINTSPR00412, PRINTSPR00413, TIGRFAMsTIGR01509

KEYWORDS Hydrolase; Peroxisome; Detoxification; Aromatic hydrocarbons catabolism; Direct protein sequencing.

SOURCE Rattus norvegicus (Norway rat)

ORGANISM Rattus norvegicus

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae;

Rattus.

REFERENCE 1 (residues 1 to 554)

AUTHORS Knehr, M., Thomas, H., Arand, M., Gebel, T., Zeller, H.D. and Oesch, F.

TITLE Isolation and characterization of a cDNA encoding rat liver cytosolic epoxide hydrolase and its functional expression in Escherichia coli

J. Biol. Chem. 268 (23), 17623-17627 (1993)

MEDLINE 93352557

PUBMED 8349641

REMARK SEQUENCE FROM N.A.

STRAIN=Sprague-Dawley; TISSUE=Liver

REFERENCE 2 (residues 1 to 554)

AUTHORS Arand, M., Knehr, M., Thomas, H., Zeller, H.D. and Oesch, F.

TITLE An impaired peroxisomal targeting sequence leading to an unusual bicompartamental distribution of cytosolic epoxide hydrolase

JOURNAL FEBS Lett. 294 (1-2), 19-22 (1991)

MEDLINE 92077134

PUBMED 1743286

REMARK SEQUENCE OF 450-554 FROM N.A., AND PARTIAL SEQUENCE.

TISSUE=Liver

COMMENT

This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and the EMBL outstation - the European Bioinformatics Institute. The original entry is available from <http://www.expasy.ch/sprot> and <http://www.ebi.ac.uk/sprot>

[FUNCTION] This enzyme acts on epoxides (alkene oxides, oxiranes) and arene oxides. Plays a role in xenobiotic metabolism by degrading potential toxic epoxides. Also determines steady-state levels of physiological mediators.

[CATALYTIC ACTIVITY] An epoxide + H(2)O = a glycol.

[SUBUNIT] Homodimer.

[SUBCELLULAR LOCATION] Cytoplasmic and peroxisomal.

[INDUCTION] By compounds that cause peroxisome proliferation such as clofibrate, tiadenol and fenofibrate.

[SIMILARITY] Belongs to the AB hydrolase superfamily. Epoxide hydrolase family.

FEATURES	Location/Qualifiers
source	1..554 /organism="Rattus norvegicus" /db_xref="taxon:10116"
gene	1..554 /gene="EPHX2"
<u>Protein</u>	1..554 /gene="EPHX2" /product="Soluble epoxide hydrolase" /EC_number="3.3.2.3"
<u>Site</u>	333 /gene="EPHX2" /site_type="active" /note="By similarity."
<u>Site</u>	495 /gene="EPHX2" /site_type="active" /note="By similarity."
<u>Site</u>	523 /gene="EPHX2" /site_type="active" /note="By similarity."
<u>Site</u>	552..554 /gene="EPHX2" /site_type="unclassified" /note="Microbody targeting signal (Potential)."

ORIGIN

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☐ 1: JC4711. epoxide hydrolase...[gi:2135082]

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LOCUS JC4711 555 aa linear PRI 17-MAR-2000
 DEFINITION epoxide hydrolase (EC 3.3.2.3) 2, cytosolic - human.
 ACCESSION JC4711
 VERSION JC4711 GI:2135082
 DBSOURCE pir: locus JC4711;

summary: #length 555 #molecular-weight 62615 #checksum 7933
 ;
 genetic: #gene GDB:EPHX2 ##cross-references GDB:371845; OMIM:132811
 #map_position 8p21-8p12 #introns 34/2; 62/3; 116/1; 179/3; 220/3;
 245/3; 277/3; 304/1; 315/3; 324/3; 353/2; 390/3; 414/3; 426/1;
 460/3; 483/3; 510/3; 530/ 2
 ;
 PIR dates: 16-Aug-1996 #sequence_revision 16-Aug-1996 #text_change
 17-Mar-2000

KEYWORDS aromatic hydrocarbon catabolism; detoxification; ether hydrolase;
 liver.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (residues 1 to 555)

AUTHORS Beetham, J.K., Tian, T. and Hammock, B.D.

TITLE cDNA cloning and expression of a soluble epoxide hydrolase from
 human liver

JOURNAL Arch. Biochem. Biophys. 305 (1), 197-201 (1993)

MEDLINE 93343630

PUBMED 8342951

REFERENCE 2 (residues 1 to 555)

AUTHORS Sandberg, M. and Meijer, J.

TITLE Structural characterization of the human soluble epoxide hydrolase
 gene (EPHX2)

JOURNAL Biochem. Biophys. Res. Commun. 221 (2), 333-339 (1996)

MEDLINE 96192049

PUBMED 8619856

COMMENT This enzyme is involved in the conversion of harmful
 epoxide-containing compounds into diols.

FEATURES Location/Qualifiers

source

1..555

/organism="Homo sapiens"

/db_xref="taxon:9606"

Protein

1..555

/product="epoxide hydrolase 2, cytosolic"

/EC_number="3.3.2.3"

ORIGIN

1 mtlraavfdl dgvlalpavf gvlgrteeal alprgllnda fqkggpegat trlmkgeitl
 61 sqwiplmeen crkcsetakv clpknsike ifdkaisark inrpmlqaal mlrkkgftta
 121 iltntwlddr aerdglaqlm celkmhfdfl iescqvgmvk pepqiykfl1 dtlkaspsev

181 vflddiganl kpardlgmvt ilvqdttdal kelekvtgiq llntpaplpt scnpsdmsgh
241 yvtvkprvrl hfvelgsgpa vclchgfpes wyswryqipa laqagyrvla mdmkgygess
301 appeieeycm evlckemvtf ldklglsqav fighdwggml vwymalfype rvravaslnl
361 pfipanpnms plesikanpv fdyglyfqep gvaaeeleqn lsrtfkslfr asdesvlsmh
421 kvceagglfv nspeepslsr mvteeeiqfy vqqfkksgfr gplnwyrnme rnkwacksl
481 grkilipalm vtaekdfvlv pqmsqhmedw iphlkrghie dcghwtqmdk ptevnqilik
541 wldsdarnpp vvskm

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